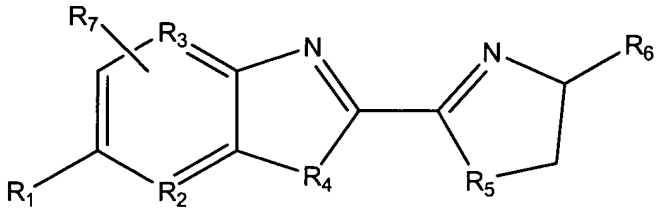
REMARKS

Applicant notes for the Examiner's convenience that claims 135 and 136 have been amended. Support for the amendments can be found throughout the specification, for example at page 14, lines 1-6; page 19, line 5; page 32, lines 9-12; and in the Examples at page 57, line 30 bridging to page 58, line 14. No new matter has been added by way of the amendments.

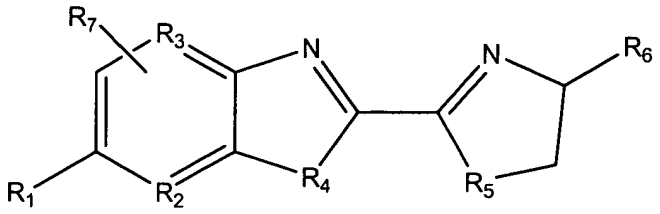
In response to the Restriction Requirement mailed March 22, 2006, Applicant provisionally elects, with traverse, the invention of claims 132-142 (Group X) directed to a D-luciferin derivative that is a substrate of a cytochrome P450 enzyme and a pro-substrate of luciferase enzyme; a D-luciferin derivative having the formula:



wherein R_1 represents hydrogen, hydroxy, C_{1-20} alkoxy or C_{1-20} alkenyloxy wherein the alkoxy and alkenyloxy are optionally substituted with halogen, hydroxy, amino, cyano, azido, or heteroaryl or aryl optionally substituted with haloalkyl; or R_1 represents C_{3-20} alkynyloxy; cycloalkoxy, cycloalkylamino, C_{1-20} alkylamino, diC_{1-20} alkylamino, C_{2-20} alkenylamino, diC_{2-20} alkenylamino, C_{2-20} alkenyl C_{1-20}alkylamino, C_{3-20} alkynylamino, diC_{3-20} alkynylamino, C_{3-20} alkynyl C_{1-20}alkylamino, or C_{3-20} alkynyl C_{2-20}alkenylamino, wherein each of the above groups are optionally substituted with halogen, hydroxy, amino, cyano, azido, heteroaryl or aryl substituted with haloalkyl; R_2 and R_3 independently represent C or N; R_4 and R_5 independently represent S; O; NR_8 wherein R_8 represents hydrogen or C_{1-20} alkyl; CR_9R_{10} wherein R_9 and R_{10} independently represent H, C_{1-20} alkyl or fluorine; R_6 represents CH_2OH; COR_{11} wherein R_{11} represents hydrogen, hydroxy, C_{2-20} alkenyl, or $-OM^+$ wherein M^+ is an alkali metal or a pharmaceutically acceptable salt; and R_7 represents hydrogen, C_{1-6} alkyl, C_{2-20} alkenyl, halogen or C_{1-6} alkoxide, provided that when R_1 is hydroxy, R_7 is not hydrogen, R_{11} is not hydroxy, R_2 and R_3 are not both carbon, and R_4 and R_5 are not both S (luciferin); when R_1 is hydrogen, R_7 is not hydrogen, R_{11} is not hydroxy, R_2 and R_3 are not both carbon, and R_4 and R_5 are not both S (dehydroluciferin); and when R_1 is hydroxy, R_7 is not hydrogen, R_6 is not CH_2OH, R_2 and R_3 are not both carbon, and R_4

and R_5 are not both S (luciferol); and a compound selected from the group consisting of luciferin 6' 2-chloroethyl ether, luciferin 6' benzyl ether, luciferin 6' 4-picolinyl ether, luciferin 6' 4-trifluoromethylbenzyl ether, luciferin 6' phenylethyl ether, luciferin 6' geranyl ether, luciferin 6' prenyl ether, luciferin 6' 2-picolinyl ether, and luciferin 6' 3-picolinyl ether. With regard to the election of a specie, Applicant provisionally elects, with traverse, the specie luciferin 6' benzyl ether. Claims 132-138 and 140-142 read on the elected specie, and claim 139 is a subset of claim 136. Reconsideration and withdrawal of the Restriction Requirement and the election of species, in view of the remarks herein, is respectfully requested.

The Restriction Requirement is traversed on the basis that the inventions are closely related. That is, claims directed to a D-luciferin derivative that is a substrate of a cytochrome P450 enzyme and a pro-substrate of luciferase enzyme; a D-luciferin derivative having the formula:



wherein R_1 represents hydrogen, hydroxy, C_{1-20} alkoxy or C_{1-20} alkenyloxy wherein the alkoxy and alkenyloxy are optionally substituted with halogen, hydroxy, amino, cyano, azido, or heteroaryl or aryl optionally substituted with haloalkyl; or R_1 represents C_{3-20} alkynyloxy; cycloalkoxy, cycloalkylamino, C_{1-20} alkylamino, diC_{1-20} alkylamino, C_{2-20} alkenylamino, diC_{2-20} alkenylamino, C_{2-20} alkenyl C_{1-20}alkylamino, C_{3-20} alkynylamino, diC_{3-20} alkynylamino, C_{3-20} alkynyl C_{1-20}alkylamino, or C_{3-20} alkynyl C_{2-20}alkenylamino, wherein each of the above groups are optionally substituted with halogen, hydroxy, amino, cyano, azido, heteroaryl or aryl substituted with haloalkyl; R_2 and R_3 independently represent C or N; R_4 and R_5 independently represent S; O; NR_8 wherein R_8 represents hydrogen or C_{1-20} alkyl; CR_9R_{10} wherein R_9 and R_{10} independently represent H, C_{1-20} alkyl or fluorine; R_6 represents CH_2OH; COR_{11} wherein R_{11} represents hydrogen, hydroxy, C_{2-20} alkenyl, or $-OM^+$ wherein M^+ is an alkali metal or a pharmaceutically acceptable salt; and R_7 represents hydrogen, C_{1-6} alkyl, C_{2-20} alkenyl, halogen or C_{1-6} alkoxide, provided that when R_1 is hydroxy, R_7 is not hydrogen, R_{11} is not hydroxy, R_2 and R_3 are not both

carbon, and R_4 and R_5 are not both S (luciferin); when R_1 is hydrogen, R_7 is not hydrogen, R_{11} is not hydroxy, R_2 and R_3 are not both carbon, and R_4 and R_5 are not both S (dehydroluciferin); and when R_1 is hydroxy, R_7 is not hydrogen, R_6 is not CH_2OH, R_2 and R_3 are not both carbon, and R_4 and R_5 are not both S (luciferol); and a compound selected from the group consisting of luciferin 6' 2-chloroethyl ether, luciferin 6' benzyl ether, luciferin 6' 4-picolinyl ether, luciferin 6' 4-trifluoromethylbenzyl ether, luciferin 6' phenylethyl ether, luciferin 6' geranyl ether, luciferin 6' prenyl ether, luciferin 6' 2-picolinyl ether, and luciferin 6' 3-picolinyl ether (claims 132-142; Group X), are related to claims directed to kits having one or more luminogenic molecules that are a cytochrome P450 substrate and a pro-substrate of bioluminescent enzyme (claims 116-131; Group IX); claims directed to methods of using a luminogenic molecule that is a cytochrome P450 substrate and a pro-substrate of bioluminescent enzyme, e.g., a luciferin derivative or a coelentrazine or a coelenterazine derivative that is chemiluminescent, e.g., for measuring the activity of a cytochrome P450 enzyme (claims 1-7, 111-115, 143, and 158-160; Group I), for measuring cytochrome P450 enzyme activity in a cell (claims 8-17, 111-115, 144-147, and 158-160; Group II), for measuring cytochrome P450 enzyme activity in animal or tissue thereof (claims 18-28, 111-115, 148, and 158-160; Group III), for measuring cytochrome P450 enzyme activity in a transgenic animal having a bioluminescent enzyme transgene (claims 29-30, 149, and 158-160; Group IV); claims directed to methods for screening a compound for its effect on cytochrome P450 activity which employ a luminogenic molecule that is a cytochrome P450 substrate and a pro-substrate of bioluminescent enzyme, e.g., a luciferin derivative or a coelentrazine or a coelenterazine derivative that is chemiluminescent (claims 31-40, 66-75, 111-115, 150, 154, and 158-160; Group V), or methods for determining the effect of a compound on cytochrome P450 enzyme activity which employs a luminogenic molecule that is a cytochrome P450 substrate and a pro-substrate of bioluminescent enzyme, e.g., a luciferin derivative or a coelentrazine or a coelenterazine derivative that is chemiluminescent, e.g., in a cell (claims 41-49, 76-88, 111-115, 151, 155 and 158-160; Group VI), animal (claims 50-58, 89-102, 111-115, 152, 156, and 158-160; Group VII) or a transgenic animal (claims 59-65, 103-113, 153, and 158-160; Group VIII).

The Restriction Requirement is also traversed on the basis that Restriction Requirements

are optional in all cases. M.P.E.P. § 803. If the search and examination of at least a portion of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims distinct or independent inventions. M.P.E.P. § 803. Moreover, it is submitted that Applicant should not be required to incur the additional costs associated with the filing of multiple divisional applications in order to obtain protection for the claimed subject matter, e.g., filing 10 divisional applications. Due to the relatedness of the subject matter of at least the claims in Group X and Groups I-IX as discussed above, those Groups can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner.

Thus, the Restriction Requirement is properly traversed. Accordingly, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

Further, Applicant's Representative respectfully request rejoinder of the claims in Groups I-VIII (methods of using a luminogenic molecule that is a cytochrome P450 substrate and a pro-substrate of bioluminescent enzyme) with the claims in Group X, upon a notice of allowable subject matter for the claims in Group X.

The requirement to elect a species is traversed on the basis that the disclosed species have a disclosed relationship, i.e., they are luciferin derivatives including those useful to detect cytochrome P450 enzymes. Therefore, withdrawal of the species election is respectfully requested.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 359-3270 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

JAMES J. CALI, ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 359-3270

Date 7/24/2006 By _____
Michael H. Haukaas
Reg. No. 57,111

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 24th day of July, 2006.

Dawn M. Pasle
Name

Dawn M. Pasle
Signature